

A polynucleotide is provided which comprises at least two repeats of a hypoxia element (HRE), wherein the hypoxia-inducible factor consensus binding sites within each of the two repeats are separated by a spacer of at least 20 contiguous nucleotides. A

two repeats are separated by a spacer of at least 20 contiguous nucleotides. The polynucleotide is also provides which comprised at least three repeats of a phosphoglycerate kinase (PGK) hypoxia response element (HRE) operably linked to an SV40 promoter or an MLV promoter. The polynucleotide may be operably linked to a nucleic acid of interest to drive expression of the NOI in a cell under hypoxic conditions.

[illegible]